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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/044,006	01/11/2002	Alexander Baguisi	21578-007	8234
7590 06/16/2004 MINTZ, LEVIN, COHEN, FERRIS, GLOVSKY and POPEO, P.C. One Financial Center			EXAMINER WILSON, MICHAEL C	
			Boston, MA 0	2111
			DATE MAILED: 06/16/2004	1

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)				
	10/044,006	BAGUISI ET AL.				
Office Action Summary	Examiner	Art Unit				
	Michael C. Wilson	1632				
The MAILING DATE of this communication ap Period for Reply	pears on the cover sheet with	h the correspondence address				
A SHORTENED STATUTORY PERIOD FOR REPL THE MAILING DATE OF THIS COMMUNICATION.  - Extensions of time may be available under the provisions of 37 CFR 1. after SIX (6) MONTHS from the mailing date of this communication.  - If the period for reply specified above is less than thirty (30) days, a rep. If NO period for reply is specified above, the maximum statutory period.  - Failure to reply within the set or extended period for reply will, by statut Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	136(a). In no event, however, may a re only within the statutory minimum of thirty will apply and will expire SIX (6) MONT te, cause the application to become ABA	ply be timely filed  (30) days will be considered timely.  HS from the mailing date of this communication.  NDONED (35 U.S.C. & 133).				
Status						
1) Responsive to communication(s) filed on 15 s	September 2003.					
2a) ☐ This action is <b>FINAL</b> . 2b) ☑ Thi	<u> </u>					
3) Since this application is in condition for allowa	3) Since this application is in condition for allowance except for formal matters, prosecution as to the ments is					
closed in accordance with the practice under	Ex parte Quayle, 1935 C.D.	11, 453 O.G. 213.				
Disposition of Claims						
4)⊠ Claim(s) <u>1-25</u> is/are pending in the application.						
4a) Of the above claim(s) <u>1-5 and 23-25</u> is/are withdrawn from consideration.						
5) Claim(s) is/are allowed.						
6)⊠ Claim(s) 6-22 is/are rejected.						
7) Claim(s) is/are objected to.	· · · · · · · · · · · · · · · · · · ·					
8) Claim(s) are subject to restriction and/o	or election requirement.					
Application Papers						
9) The specification is objected to by the Examination	er	·				
10) The drawing(s) filed on is/are: a) acc		v the Examiner				
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).						
Replacement drawing sheet(s) including the correct		• •				
11) The oath or declaration is objected to by the E						
Priority under 35 U.S.C. § 119						
12) Acknowledgment is made of a claim for foreign	a priority under 25 H.S.C. &	110(a) (d) as (f)				
a) ☐ All b) ☐ Some * c) ☐ None of:	i priority under 33 0.3.0. §	119(a)-(u) 01 (1).				
1.☐ Certified copies of the priority documents have been received.						
2. Certified copies of the priority documents have been received in Application No						
3. Copies of the certified copies of the priority documents have been received in this National Stage						
application from the International Bureau (PCT Rule 17.2(a)).						
* See the attached detailed Office action for a list		eceived.				
	·					
Attachment(s)						
1) Notice of References Cited (PTO-892)	4) Interview Sur	mmary (PTO-413)				
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/	Mail Date				
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4-5&11-8-02:1-13-4.	5) Notice of Info 6) Other:	ormal Patent Application (PTO-152)				
U.S. Patent and Trademark Office PTOL-326 (Rev. 1-04) Office A	ction Summary	Part of Paper No./Mail Date 060804				

#### **DETAILED ACTION**

#### Election/Restrictions

Applicant's election without traverse of Group II, claims 6-22, in the reply filed on 9-15-04 is acknowledged.

Claims 1-5 and 23-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9-15-04.

Claims 6-22 are under consideration in the instant office action.

#### Oath/Declaration

The oath or declaration is defective because it is not signed. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by number and filing date is required. See MPEP §§ 602.01 and 602.02.

#### Specification

It is noted that the background of the invention does not include any of the numerous references known in the art relating to methods of isolating embryonic avian cells, transfecting the cells and transplanting the cells into a recipient embryo as claimed.

Reference to the US Patent application on pg 17, lines 16, will need updating as necessary.

## Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

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person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 6-22 require introducing a nucleic acid molecule into the genome of an avian species.

For enablement purposes the phrase "introducing a nucleic acid molecule into the genome of an avian species" in the preamble of claim 6 bears patentable weight because each limitation must have one enabled use. The steps of the method do not require making an avian or that the nucleic acid is incorporated into the genome any avian species; however, "introducing a nucleic acid molecule into the genome of an avian species" bears patentable weight under enablement because each limitation must be enabled for at least one intended use.

In this case, introducing a nucleic acid molecule into the genome of an avian species is for making genetically altered avians having improved quality, a model of human disease, disease resistance avians or to conserve endangered species using a chicken as a "universal recipient" (pg 6, lines 7-13). However, the specification does not provide adequate guidance for one of skill to introducing a nucleic acid molecule into the genome of an avian. The

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specification does not provide adequate guidance for one of skill to make a avian with improved quality, that is a model of human disease, that is disease resistant or that is a "universal recipient" because these all require introducing a nucleic acid molecule into the genome of an avian.

The claims require transfecting gonadal cells with a nucleic acid molecule prior to being introduced into a recipient embryo. Transfecting avian PGCs cells with a nucleic acid and transplanting the cells into a recipient embryo was known in the art. Stage 11 PGCs had been isolated from chickens, transduced with retrovirus, and immediately injected into the vasculature of Stage 15 chick embryos to obtain germline transmission of a transgene (Vick, Proc. R. Soc. Lond., 1993, Vol. 251, pg 179-182). Although manipulated embryos that hatched were observed to produce offspring of the donor germline, F<sub>1</sub> offspring lost their ability to transmit the donor DNA as they matured (Proudman, 2001, Biotechnology in Animal Husbandry, Vol. 5, pg 283-299, Renaville and Burny (eds.) Kluwer Academic Publishers; pg 290, 2<sup>nd</sup> full ¶). Thus, the nucleic acid was not introduced into the genome of the avian; the nucleic acid was introduced episomally. Therefore, it was unpredictable whether transfected gonadal cells with a nucleic acid molecule introduced into a recipient embryo would result in the nucleic acid molecule being introduced into the genome of an avian at the time of filing.

The art did not teach how to make a transgenic avian whose genome comprised an exogenous transgene using transfected avian gonadal cells introduced into recipient avian embryos. For example, Mohammed (1998,

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Immunotechnology, Vol. 4, pg 115-125) states despite discussions of using hens for the production of recombinant human antibodies (rhAb) and attempts to do so, it had never been demonstrated. Mohammed transfected a lymphoblastoid cell line with a retrovirus encoding a rhAb, injected the cells into a chicken and obtained expression of the rhAb in the egg yolk and sometimes the egg white (pg 116, col. 1, 2<sup>nd</sup> ¶; col. 2, 1<sup>st</sup> full ¶). Mohammed did not teach how to obtain the same results using transfected blastodermal cells.

The art taught that avian gonadal cells could not be transfected and cultured over a period of time while maintaining their germline competence.

Ivarie (Trends in Biotechnology, Jan. 2003, Vol. 21, pg 14-19) taught that the complex process by which a bird makes and lays eggs makes the production of transgenic birds materially distinct and separate from those of mice. Ivarie cites Pain and teaches cultured, non-transfected, stage X blastodermal cells provided germline transmission; however, the cultured, transfected, stage X blastodermal cells did not maintain their germline competence. No transgenic birds have been made using cultured, transfected stage X blastodermal cells. The biggest obstacle to overcome in making transgenic birds whose genomes' comprise an exogenous transgene using transfected embryonic gonadal cells is the loss of germline competence during culture of transfected gonadal cells (Ivarie, pg 14, col. 2, 3<sup>rd</sup> full ¶, 1<sup>st</sup> sentence; pg 17, col. 1, 2<sup>nd</sup> full ¶, last two sentences; pg 17, sentence bridging col. 1-2; pg 17, col. 2, last sentence). Therefore, transfected avian gonadal cells were known to not maintain their

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germline competency and could not be used to make transgenic avians whose germ cells comprise the transgene or that expressed a heterologous protein.

While the specification teaches making chimeric chickens, the chimeric chickens were not made with transfected donor gonadal cells (Example 4, pg 19-26, especially pg 20, lines 4-16; Example 5, pg 28, lines 1-11). The specification does not provide the guidance required to overcome the unpredictability in the art for one of skill to determine how to transfect gonadal cells that maintain their germline competency upon being transplanted into a recipient embryo and make transgenic avians having a genome comprising the transgene. Nor does the specification provide any working examples of making transgenic avians using transfected gonadal cells as claimed. Therefore, the specification does not overcome the unpredictability in the art at the time of filing. It would have required one of skill in the art to determine the parameters required to transfect gonadal cells such that a transgenic avian having a genome with the transgene as claimed would be produced as opposed to maintaining the transgene episomally as shown by Li (cited above).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 6 is indefinite because it does not clearly set forth the steps of the claim. The metes and bounds of what applicants consider "isolated gonadal cells" cannot be determined. It appears that the claim may require transfecting the gonadal cells *in vitro* or a step of "isolating" the gonadal cells that involves separating the gonadal cells from other cells. However, it is unclear whether gonadal cells in an embryo that have been chosen for transfection and isolated in an injection devise are also encompassed by the claim. The step of "contacting" is also unclear. It is unclear if the step of "contacting" a cell with a nucleic acid sequence is limited to transfecting or if contacting an isolated gonadal cell with a nucleic acid molecule in an embryo of another breed of chicken is encompassed by the phrase. The phrase "to yield transfected gonadal cells" is an intended use and may not occur because the claim does not require a step of transfecting and because contacting a cell with a nucleic acid molecule may not result in transfection.

In claim 6, the scope of the preamble is not commensurate with the body of the claim. The preamble requires introducing a nucleic acid molecule into the genome of an avian but the body of the claim does not require producing any avian, specifically one that have the nucleic acid molecule in its genome.

The metes and bounds of when a population of isolated gonadal cells comprises at least 0.5%, 1%, 50% or 90% primordial germ cells (PGCs) (claims 7-10) cannot be determined. It is unclear what criteria applicants use to define PGCs. More importantly, it is unclear if the percentage of PGCs must occur during the isolation process (i.e. a particular stage in which the percentage of

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PGCs is increased in the embryonic gonad) or when the gonadal cells are transferred into the recipient embryo (i.e. after PGCs have been preferentially cultured or separated from non-PGCs).

In claims 11, 12, 15 and 16, the staging of embryos is unclear. It is unclear if applicants are using the Hamburger & Hamilton (H & H) or the Eyal-Giladi method of staging. In particular, if applicants are using the H & H method, the specification uses incorrect days to describe the stages. Pg 9, line 10, describes stage 31-34 as day 7-8 after incubation (after being layed), which is correct (H & H, 1951, J. Morph. Vol. 88, pg 49-92, see pg 62-63). However, pg 2, lines 14-15, describe stage 29-36 as day 7.5, which H & H describe stage 29-36 as 6-10 days. Pg 11, line 9, describes stage 7-8 as 24 hours, which H & H describes stage 7-8 as 23-29 hours; 24 hours does not include stage 8 according to H & H (H & H pg 55). Pg 11, line 11, describes stage 11-13 as 48 hours, while H & H describes stage 11-13 as 40-49 hours. Stage 11 does not include 48 hours according to H & H (pg 55). Pg 2, lines 23-24, pg 11, line 14, pg 11, lines 17-19, pg 11, lines 20-21 and pg 11, line 25, all have errors if applicants intend to cite the H & H method of staging. However, because of the difference in the description of staging in the specification as compared to the H & H method, it cannot be determine whether applicants are attempting to redefine the stages or if the specification has errors. As such, reference to stages in claims 11, 12, 15 and 16 is unclear. One of skill would not been able to determine whether applicants were attempting to be their own lexicographer or whether the description of the stages was in error.

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The term "derived" in claims 13 and 14 is unclear. It is unclear if the term refers to "isolated" cells or eggs or if the term is limited to cells or eggs that have evolved or been obtained from a particular process. The term is also unclear as it relates to chimeric embryos, e.g. quail-chicken embryos.

The term "fertilized avian egg" in claims 15, 16, 18, 19 and 20 lacks antecedent basis in claim 6. Literal support is required when using "said. Claim 6 requires a fertilized <u>recipient</u> avian egg.

Reference to transferring "said transfected gonadal cells" in claims 19-21 is indefinite because claim 6 does not ever require producing transfected gonadal cells or transfecting gonadal cells. The phrase "to yield transfected gonadal cells" in claim 6 is an intended use and is not a clear positive step indicating the cells contacted with a nucleic acid molecule have been transfected or a clear positive step indicating the contacting is transfecting.

For art purposes the phrase "introducing a nucleic acid molecule into the genome of an avian species" in the preamble of claim 6 does not bear patentable weight because the steps of the method merely require contacting a population of isolated gonadal cells obtained from a chick embryo with the nucleic acid to yield transfected gonadal cells and transferring the transfected gonadal cells to a fertilized recipient avian egg. The steps of the method do not require making an avian or that the nucleic acid is incorporated into the genome any avian species. Therefore, "introducing a nucleic acid molecule into the genome of an avian

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species" is an intended use and does not bear patentable weight because it does not have to occur.

### Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
- (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors

Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology

Technical Amendments Act of 2002 do not apply when the reference is a U.S.

patent resulting directly or indirectly from an international application filed before

November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

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Claims 6-12, 15, 16 and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Petitte (US Patent 6,333,192, filed Aug. 9, 1999) and supported by Hamburger (1951, J. Morphol. Vol. 88, pg 49-92).

Petitte taught isolating PGCs and stromal cells from the gonads of stage 30 avian embryos, transfecting the PGCs in vitro, and transplanting the PGCs into a recipient avian embryo (col. 7, lines 18-42; col. 4, lines 57-67). The percentage of PGCs at day 0 was 100% (Figure 1). The recipient avian embryos are implanted with the PGCs prior to 2 or 3 of incubation, and preferably prior to day 1 of incubation (col. 7, lines 36-40). Day 1 (24 hours) of incubation is equivalent to H & H stage 7 as claimed (see pg 55 of Hamburger). Day 2 (48 hours) of incubation is equivalent to H & H stage 13 as claimed (see pg 56 of Hamburger). Inherently, 50% of the recipient embryos were of the same sex as the donor PGCs (claim 22).

Claims 6-10, 16, 21 and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Tsai (US Patent 6,140,118, filed 8-11-99).

Tsai taught isolating blastodermal cells from the area pellucida of gonads of avian embryos, transfecting the blastodermal cells, and transplanting the blastodermal cells into a recipient avian embryo that was incubated for 18 hours (col. 5, lines 17-20, col. 6, lines 18-19, 39-50). The percentage of PGCs in the blastodermal cells isolated or in the blastodermal cells transplanted into the recipient embryo cannot be determined by the patent office. Since the patent office does not have the ability to determine the percentage of PGCs in the

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population of cells isolated or the cells transplanted, without evidence to the contrary, the percentage was at least 90% as claimed because they were grown to confluency and separated from adherent cells (col. 5, lines 43-48). Inherently, 50% of the recipient embryos were of the same sex as the donor PGCs (claim 22).

Claims 6-13, 16, 17 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Hong (Transgenic Res. 1998, Vol. 7, pg 247-252).

Hong taught isolating PGCs from stage 29 (H & H) White Leghorn embryos, transfecting them and injecting them into day 2.5 (stage 17 H & H) embryos. Inherently, 50% of the recipient embryos were of the same sex as the donor PGCs (claim 22).

Claims 6-10, 13, 16-18 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Vick (Proc. R. Soc. Lond. 1993, Vol. 251, pg 179-182).

Vick taught isolating primordial germ cells (PGCs) from the germinal crescent cells of a stage 11 White Leghorn chicken embryo, transfecting the cells with a retroviral vector and transplanting the cells into a stage 15 Rhode Island Red chicken embryo. While Vick taught the mean number of PGCs per germinal crescent was 98 (pg 180, col. 2, line 3-4), Vick did not teach the percentage of PGCs in the population of cells isolated from the germinal crescent. However, the percentage of PGCs in the population of cells isolated from the germinal crescent taught by Vick was inherently at least 90% as claimed (claim 10). Vick

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taught separating the PGCs from other cells such as yolk cells by centrifugation (pg 180, col. 1, lines 6-8). Vick stated the "PGCs were cultured" and does not state other cell types were included. It is noted that the PGCs' viability was determined throughout the isolation process (pg 180, Table 1 and Figure 1); however, this data does not relate to the percentage of PGCs in the cells isolated from the embryo as claimed. Since the patent office does not have the ability to determine the percentage of PGCs in the population of cells isolated from the germinal crescent, without evidence to the contrary, the percentage was at least 90% as claimed because Vick taught separating PGCs from yolk cells by centrifugation and specifically refers to culturing PGCs without referring to contaminating cells. Inherently, 50% of the recipient embryos were of the same sex as the donor PGCs (claim 22).

#### Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.

- Resolving the level of ordinary skill in the pertinent art.
- 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 14, 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pardue (US Patent 6,354,242, filed 3-23-00) in view of Petitte (US Patent 6,333,192, filed Aug. 9, 1999).

Pardue taught isolating germ cells from the gonads of stage 27-28 turkey embryos, and transplanting the germ cells into a recipient chicken embryo (col. 6, lines 41-51). The recipient embryos could be optionally sterilized prior to transplantation (col. 1, line 53-55). Inherently, 50% of the recipient embryos were of the same sex as the donor germ cells (claim 22). Pardue did not teach contacting the germ cells with a nucleic acid sequence to yield a transfected gonadal cell.

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However, Petitte taught isolating PGCs and stromal cells from the gonads of stage 27-28 avian embryos, transfecting the PGCs in vitro, and transplanting the PGCs into a recipient avian embryo (col. 7, lines 18-42; col. 4, lines 57-67).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to isolate germ cells from the gonad of a turkey embryo and transplant the germ cells into a chicken embryo as taught by Pardue, wherein the turkey germ cells were transfected prior to transplantation as taught by Petitte. One of ordinary skill in the art at the time the invention was made would have been motivated to transfect the turkey germ cells with a nucleic acid sequence encoding a marker protein prior to transplantation into a chicken embryo to detect the turkey cells in the chimeric embryo.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Claims 6, 14, 19, 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pardue (US Patent 6,354,242, filed 3-23-00) in view of Petitte (US Patent 6,333,192, filed Aug. 9, 1999) as applied to claims 6, 14, 19 and 22 and further in view of Aige-Gil (1991, Res. Vet. Sci. Vol. 50, pg 139-144).

The combined teachings of Pardue and Petitte taught isolating germ cells from the gonads of stage 27-28 turkey embryos, transfecting the germ cells with a nucleic acid sequence, sterilizing the recipient embryo prior to transplantation and transplanting the germ cells into the recipient chicken embryo (Pardue, col. 6, lines 41-51; col. 1, line 53-55; Petitte, col. 7, lines 18-42; col. 4, lines 57-67).

The combined teachings of Pardue and Petitte did not teach sterilizing the recipient embryo with busulphan.

However, Aige-Gil taught busulphan sterilized avian the PGCs of avian embryos (pg 143, Table 3).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to isolate germ cells from the gonad of a turkey embryo, transfect the turkey germ cells, sterilize a recipient chicken embryo and transplant the germ cells into the chicken embryo as taught by the combined teachings of Pardue and Petitte, wherein the recipient chicken embryo is sterilized using busulphan as taught by Aige-Gil. One of ordinary skill in the art at the time the invention was made would have been motivated to sterilized the recipient embryo with busulphan as taught by Aige-Gil instead of ultraviolet light as taught by Pardue because Aige-Gil states busulphan provides the advantage of acting predominantly on stem cells while ultraviolet light would act generically on all cells in the embryo.

Thus, Applicants' claimed invention as a whole is prima facie obvious in the absence of evidence to the contrary.

#### Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at 571-272-0738.

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Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAELWILSON PRIMARY EXAMINER